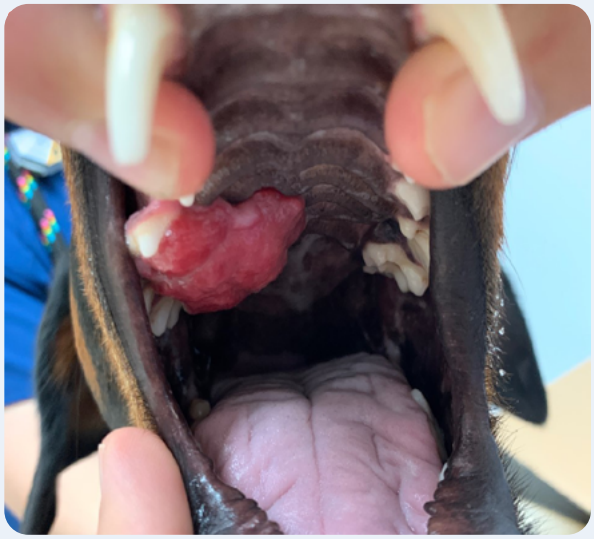
Genomic Case Profile: Remmy

SearchLight DNA™ Guides Treatment Planning

OVERVIEW

- Remmy, a vibrant young Doberman Pinscher, had a mass along the hard palate that was histologically identified as a poorly differentiated neoplasm.
- A SearchLight DNA test revealed a BRAF point mutation, suggesting sensitivity to multiple targeted therapies including trametinib.
- In Remmy's case, SearchLight DNA was able to give a therapeutic indication based on a mutation identified within the tumor, even though the mutation is usually associated with other tumor types.
- Remmy's tumor experienced significant shrinkage with trametinib, and Remmy did not have any side effects associated with this drug.



Remmy is a 3-year-old male neutered Doberman Pinscher who was seen by his primary care veterinarian for a 1-week history of oral bleeding. Upon examination, the source of the blood was determined to be the eroded surface of a fast-growing tumor. The mass was then removed, although the entirety of the tumor could not be excised due to the high vascularity (many blood vessels) at the base of the mass. The mass was histologically identified as a poorly differentiated neoplasm, with infrequent mitoses (2/10 HPF), no angiolymphatic invasion, and extending to the inked histologic margins. Oral rhabdomyosarcoma was the favored differential, although other differentials included granular cell tumor, amelanotic melanoma, and fibrosarcoma/undifferentiated sarcoma.

Remmy's mass was noted to have regrown within a month, by the time he was seen by his oncologist. A large, approximately 5 cm pink, broad-based mass was noted during the oral exam, although his lymph nodes and the remainder of his physical exam were unremarkable. Several therapeutic options were discussed, including a large surgery to remove the mass (partial maxillectomy), either alone or ideally with adjuvant radiation therapy; high-dose radiation therapy (stereotactic radiation); genomic profiling with SearchLight DNA with possible targeted therapeutic indications; or palliative care.

SearchLight DNA was pursued, and two mutations were identified: BRAF point mutation (V588G, aka BRAF V595E) and CDKN2B copy number loss (deletion). BRAF is a gene that encodes a protein belonging to the RAF family of serine/threonine/protein kinases. BRAF plays a role in regulating the MAP kinase/ERK signaling pathway which affects cell division, differentiation, and secretion. Mutations in this gene are well-characterized cancer-driving mutations that occur in many canine and human cancers. In dogs, the BRAF mutation found in Remmy's tumor commonly occurs in canine transitional cell carcinoma and prostate cancer, but also occurs at various frequencies in other cancers, such as melanoma, histiocytic sarcoma, and peripheral nerve sheath tumor. In humans, this mutation corresponds to the BRAF V600E mutation and is considered a recurrent, activating mutation seen in human melanoma, thyroid cancer, colorectal cancer, and hematologic malignancies; it also occurs at lower frequency in sarcomas including rhabdomyosarcoma and peripheral nerve sheath tumor. The CDKN2B deletion identified in this sample has also been found in many canine and human cancers, including sarcomas.

The BRAF mutation identified in Remmy's tumor suggested sensitivity to several targeted therapies, only one of which—trametinib—is currently available at veterinary compounding pharmacies. Trametinib is an inhibitor of MEK1/MEK2 that is FDA-approved as a single agent for the treatment of human BRAF V600E/K mutant melanoma; when combined with dabrafenib (a BRAF inhibitor that is currently unavailable at veterinary compounding pharmacies), trametinib is also indicated for BRAF V600E mutant non-small cell lung cancer and BRAF V600E mutant anaplastic thyroid cancer. In dogs, cancer cell line studies have shown sensitivity to trametinib, with the majority of trametinib-sensitive cell lines containing mutations in MAP kinase pathway members, including BRAF. Remmy was started on trametinib in the face of macroscopic disease, and he had a significant reduction in tumor size (~50%) after just 1 month of trametinib. He also did not experience any side effects from trametinib, which was administered to him orally once daily by the owner at home. Unfortunately, Remmy's tumor regrew 3 months later (4 months after starting trametinib therapy). Still, SearchLight DNA was able to provide an attainable and comfortable therapeutic option which provided Remmy with several more months of good quality of life and no toxicities from therapy.

If you have a case you would like to share or discuss with our scientists, schedule a consultation.

Schedule a Consultation